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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/020,450	12/14/2001	Guy Michael Miller	346392000900	1698

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EXAMINER	
SPIVACK, PHYLLIS G	
ART UNIT	**PAPER NUMBER**
1614	

DATE MAILED: 05/25/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/020,450	MILLER ET AL.	
	Examiner	Art Unit	
	Phyllis G. Spivack	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 February 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4,6,9-23,33-38,42-47 and 51-72* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4,6,9-23,33-38,42-47 and 51-72* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *2-9-05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Applicants' Request for Continued Examination (RCE) filed February 9, 2005 is acknowledged and accepted. Claims 1, 2, 4, 6, 9-23, 33-38, 42-47 and 51-72 remain under consideration.

Information Disclosure Statements filed February 2, 2004 and February 9, 2005 are further acknowledged and have been reviewed.

A new title is noted.

Claims 1, 2, 4, 6, 9-23, 33-38, 42-47 and 51-62 were rejected in the last Office Action under 35 U.S.C. 102(e) as being anticipated by Wechter, W.J., U.S. 2004/0058987. It was asserted Wechter teaches methods for treating and/or ameliorating the symptoms of a cerebral ischemic condition in a mammalian subject comprising administering a non-alpha tocopherol enriched tocopherol composition to reduce neuronal damage related to said cerebral condition.

Applicants argue nowhere in the specification of Wechter 2004/0058987 is the term "cerebral ischemic condition" used and the specification fails to describe a method for treating and/or ameliorating a symptom of neuronal damage associated with a cerebral ischemic condition by administering a non-alpha tocopherol enriched tocopherol composition. Further, Applicants urge the filing date of Wechter, September 12, 2003, is later than the effective filing date of the instant application.

Claims 1, 2, 4, 6, 9-23, 33-38, 42-47 and 51-62 were rejected in the last Office Action under 35 U.S.C. 102(e) as being anticipated by Wechter, W.J., U.S. 2004/0058986. It was asserted Wechter teaches methods of treating and/or

ameliorating the symptoms of a noncardiovascular tissue ischemic condition comprising administering a non-alpha tocopherol enriched tocopherol composition.

This rejection of record under 35 U.S.C. 102(e) is withdrawn because the reference is not drawn to a cerebral ischemic condition.

In the last Office Action claims 1, 2, 4, 6, 9-23, 33-38, 42-47 and 51-62 were rejected under 35 U.S.C. 103 as being unpatentable over Wechter, W.J., US 2004/0029954. It was asserted Wechter broadly claims methods of treating any ischemic condition comprising administering a composition comprising tocopherols, at least 50% of which are gamma-tocopherol. Examples of ischemic conditions are recited in the claims of US 2004/0029954, pages 21-22.

A brief discussion in the Merck Manual was supplied to support the Examiner's position that an improvement in blood supply to the brain would reasonably result in a reduction of neuronal damage.

Applicants argue the specification of 2004/0029954 does not describe or support the subject matter of the claims set forth in this Wechter application as filed on February 21, 2003. Further, the filing date of Wechter is later than both the filing date and the priority dates of Applicants' instant application and thus the cited subject matter of the reference cannot be said to render obvious Applicants' claimed invention. Further, Applicants urge the assertion that an improvement in blood supply to the brain would result in a reduction of neuronal damage associated with ischemia lacks basis in the specification or in objective reality. In this regard Applicants' argument is solely directed to reperfusion.

Applicants' arguments in response to the rejections based on two Wechter references set forth *supra* have been given careful consideration. A collective response to each of the arguments to these rejections of record follows. Most of Applicants' points are repeated in each argument for each reference.

The Examiner is not able to express an opinion on the validity or patentability of a patent or pending patent. See MPEP 1701. Every patent is presumed to be valid, 35 U.S.C 282, first sentence. Accordingly, the Examiner may not express any opinion as to adequate enablement in an allowed or co-pending application. The rejection of record relating to Wechter 2004/0058987, *supra*, meets the criteria of anticipation in that the drug, a concept and means of administration are presented. Claims 1 and 15-17, pages 21-22, in Wechter, 2004/0029954, recite methods of treating an ischemic condition, such as a condition associated with the brain or nervous system, wherein at least 50% of a tocopherol composition comprises γ-tocopherol. Therefore, treatment of neuronal damage associated with cerebral ischemia comprising administering a non-alpha tocopherol enriched composition is at least suggested. Although it is acknowledged reperfusion injury results in neuronal damage, in other circumstances, such as following a vascular spasm, an improvement in blood supply would reasonably be expected to result in a reduction of neuronal damage.

Accordingly, an expectation of success is set forth by the subject matter in Wechter, 2004/0029954. The rejection of record under 35 U.S.C. 103 is maintained over claims 1, 2, 9-23 and 51-66. The rejection of record under 35 U.S.C. 102(e) is maintained and presently extended to claims 63-72.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 4, 9-14, 33-38, 51-63 and 67-69 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kobayashi et al., Free Rad. Res.

Kobayashi teaches the administration of antioxidants, such as α-tocopherol and its analogs, to protect neuronal cells against cytotoxicity as a result of cerebral ischemia. In a laboratory model using HT-4 cells, a rat hippocampal cell line, β-tocopherol, in addition to α-tocopherol, was shown to protect these neuronal cells from glutamate-induced cytotoxicity. The cytotoxicity was characterized by loss of cell viability. See Figure 2, page 119. In view of Kobayashi's teaching, one skilled in the neurology art would have been motivated to administer a β-tocopherol enriched tocopherol composition to treat neuronal damage associated with cerebral ischemia. Such would have been obvious because oxidative stress is implicated in cerebral ischemia. A decrease or lack of blood supply to the brain results in neuronal damage. Conditions such as occlusion, thromboemboli or spasm are known to cause cerebral ischemia. The determinations of an optimal concentration and an optimal dosage of β-tocopherol are parameters well within the purview of those skilled in the art.

Claims 1, 2, 4, 6, 9-23, 33-38, 42-47 and 51-72 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chabrier de Lassauniere et al., U.S. Patent 6,297,281.

Chabrier teaches the administration of two active ingredients in combination to treat cerebral ischemia. These are an NO synthase inhibitor and a trap of reactive forms of oxygen that collectively provide a highly protective effect on focal cerebral ischemia. See column 4, lines 51-53, where non-alpha tocopherols are disclosed as examples. The claims differ in that Chabrier teaches a two agent combination to achieve a therapeutic effect. One skilled in the art would have been motivated to administer a nitric oxide inhibitor in combination with a mixture of tocopherols in view of Chabrier's teaching. Such would have been obvious because nitric oxide mediates neuronal cell death after focal cerebral ischemia. See column 1, lines 65-66. Further, the open language of the present claims allows for the administration of additional active agents to provide a therapeutic effect. The determinations of an optimal concentration and an optimal dosage of β-tocopherol are parameters well within the purview of those skilled in the art.

The rejection in the last Office Action of claims 1, 2, 4, 6, 9-23, 33-38, 42-47 and 51-62 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 2, 11-13, 22, 31-33, 42, 53-57 and 98 in co-pending application 10/017717 is maintained following Applicants' request to hold this rejection in abeyance and is presently extended to include claims 63-72.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Phyllis G. Spivack whose telephone number is 571-272-

0585. The Examiner can normally be reached Mondays to Fridays from 10:30 AM to 7 PM.

If attempts to reach the Examiner by telephone are unsuccessful after one business day, the Examiner's supervisor, Chris Low, can be reached at telephone number 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Phyllis Spivack

Phyllis G. Spivack
Primary Examiner
Art Unit 1614

May 22, 2005

PHYLLIS SPIVACK
PRIMARY EXAMINER